THE AMOUNT OF MALARIA DEPENDS ON THE NUMBERS OF THE CARRIERS

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PREFATORY NOTE

THIS pamphlet consists of three sections of my book *The Prevention of Malaria* (Murray, 1910; second edition, 1911). Republication of these has been thought advisable, because even good workers on malaria still seem to find a difficulty in understanding the principles summarised at the end of the pamphlet.

The mathematical treatment employed is quite elementary and will be easily grasped by anyone who takes the trouble. The second edition of *The Prevention* concluded with a much more elaborate version, but this was so hurriedly written that I find revision of it impracticable (though the equations were usually sound enough). The Royal Society subsequently published a much more worthy version for mathematical readers by Dr. Hilda P. Hudson and myself (*Proceedings*, vol. 92, 1916, and vol. 93, 1917), and we are now preparing a little book on the subject.

The lay reader should be informed that *Plasmodium* is the scientific name of the group of parasites three species of which cause malarial fever in human beings, and are carried from man to man by some, but not by all, species of the sub-family *Anophelina* of the *Culicidæ* or mosquitoes.

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Some Definitions.—We are practically therefore almost sure that infection with the parasites of malaria occurs in nature only through the bites of mosquitos—probably only of certain species of Anophelines. But this statement is not nearly sufficient for all the purposes of prevention, and we must discuss the subject in much greater detail. Why does the disease vary in amount from place to place, or even in the same place from season to season, or year to year? Why does it disappear from some countries and appear in others? The whole subject of the prevention of malaria is based upon a rational study of these questions, and the reader who is called upon to undertake such work must exert himself to consider them thoroughly. We must first have clear ideas upon the following points:—

(1). The cases of malarial fever which occur within a given locality belong, of course, to two classes, the *indigenous cases* and the *imported cases*. The first are those who were infected within the locality; the latter, those who were infected outside it, but who, after immigration, remain infected within it. The latter class may be very numerous in military stations, hill stations, and sanatoria. But they also abound in many villages of which the inhabitants are given to working elsewhere during the malarious months; and among bands of immigrant workmen. On the other hand, in small towns and villages with fixed populations most of the cases are apt to be indigenous ones. It is often difficult to determine the proportion of each class because many of the imported cases may be reinfected within the area

of observation, while many of the indigenous cases may have emigrated since infection.

(2). By the *malaria rate* of a locality I mean the percentage of persons who contain plasmodia at some given moment. We may divide this into the *indigenous malaria rate* and the *imported malaria rate.* The former may also be called the malarial *endemicity* of the place.

(3). By the *malaria index*, or *endemic index*, of a locality I mean the percentage of persons in whom any *evidence* of malarial infection was *found* at some given moment. It will be clear to medical men that such evidence cannot generally be found in all the cases of malaria in a locality—many may contain plasmodia without showing them or any objective symptoms of them. Conversely, many people may show evidence of past infection, such as enlarged spleen, without containing plasmodia at the moment. We may divide the endemic (or malaria) index into *the adult*, *the juvenile* and *the infantile endemic index.*[1]

(4). By the daily, monthly or annual *inoculation rate* of a locality I mean the percentage of persons who were inoculated or reinoculated by mosquitos during the day, month or year referred to.

(5). When we talk of the *amount of malarial fever* in a locality we generally refer to the total malaria rate in it. When we talk of the *amount of malaria* in it we generally mean its indigenous malaria rate. When we say that a place or a season is very *malarious*, we mean that the inoculation rate is very high for that place or season.

[1] The term "endemic index" was first used by Stephens and Christophers to denote the percentage of children showing the parasites in the blood, but the above definition is more correct.

(6). By the *malarial case mortality* we mean, of course, the proportion of infected persons who die of the disease.

(7). By the *malarial mortality* we mean the proportion of the total population who die of the disease.

(8). I use the word *ratio* to denote a proportion, and the word *rate* to denote a percentage. The latter is obtained by multiplying the former by one hundred.

Conditions required for the Production of New Infections in a Locality.—From what has been written already it will appear that new infections can occur in a locality only if all the following conditions exist:—

(1). That a person whose blood contains a sufficient number of gametids (sexual forms) is living in or near the locality.

(2). That an Anopheline capable of carrying the parasites sucks enough of that person's blood.

(3). That this Anopheline lives for a week or more afterwards under suitable conditions—long enough to allow the parasites to mature in it.

(4). That it next succeeds in biting another person who is not immune against the disease or is not protected by quinine.

To these we must now add the following principle:—

(5). That few or no new infections will occur in a community unless the persons with gametids in their blood and the carrying Anophelines are sufficiently numerous.

This last proposition is the basis of the public prevention of malaria. Although tacitly admitted, it is never properly discussed in the monographs, and the reader must therefore examine it here in detail and as precisely as possible.

Let us suppose that we have to do with a population of 1,000 people living over an area in which indigenous malaria does not exist; and suppose that one of these people is an

imported case with suitable gametids in his blood. Next, suppose that a single suitable Anopheline is liberated within the area. What are the chances that this insect will ever cause a new infection?

First, we observe that not every mosquito can succeed in biting human beings at all: suppose that the chances are 3 to 1 against this happening. Next, we observe that as there is only one infected person among the 1,000 people in the place, and as the particular Anopheline liberated in the area may bite any one of these people, the chances are 999 to 1 against its happening to bite the patient, even if it succeeds in biting at all. That is, altogether, the chances against its biting the patient are 3,999 to 1. But suppose that this has happened. It must now live for a week or more afterwards, and not all mosquitos live so long. Suppose that the chances are 2 to 1 against this particular Anopheline living long enough to mature the parasites in it—so that the chances are 11,999 to 1 against the Anopheline reaching the infective stage. But it must now bite a second person. Suppose that the chances against this are, again, 3 to 1. Thus the total chances against this Anopheline inoculating another person will be something like 48,000 to 1. In other words, if instead of liberating a single Anopheline within the area of observation we had liberated 48,000, the chances are that only one of these would succeed in biting the patient, and would also live long enough to become infective and to bite a second person. Of course, by bad luck, so to speak, a larger proportion of the insects might succeed in this; but, on the other hand, by good luck, none at all might succeed. Such calculations, though obviously based on conjectural data, yet suffice to show the absurdity of supposing that the presence of a few Anophelines must cause an epidemic of malaria.

Or we may consider the subject as follows:—Suppose that 48 Anophelines on the average live near the infected person. Then, if the conjectural data are sound, 1/4 of these, or 12,

will succeed in biting him; 1/3 of these, or 4, will live for a week or more; and only 1/4 of these, or 1, will succeed in biting another person. If 48 Anophelines live near each one of the 999 healthy people, there will be 47,952 Anophelines which can bite only healthy people, and which cannot therefore cause new infections. Thus, on the average, only 1 out of 48,000 Anophelines will succeed in infecting another individual.

If instead of only one person with gametids in the blood there are 2, 3, 4 . . . or more in the locality, then if there are 48 Anophelines on the average to each person, 2, 3, 4 . . . or more new infections may be caused. Thus, obviously, the number of new infections in a locality, that is, the *inoculation rate*, depends on two factors (other things being equal), namely, the number of Anophelines and the number of previously infected persons in the locality.

It is useful to put these thoughts into simple symbolic language. Let p denote the human population of the locality; mp the number of malaria-infected persons; and imp the number of these with gametids in the blood. Here m and i are fractions, since mp is less than p, and imp less than mp. Also m may vary from 0 to 1, since the number of infected persons may be anything from zero to the whole population. The fraction i, being the proportion of infected persons with gametids in their blood at the moment of enquiry, may be put at 1/4, or may be much less.

Again, let a denote the number of Anophelines (of some malaria-bearing species) to each human being — so that ap denotes the total number of Anophelines in the locality, and $aimp$ the number of Anophelines compared with the number of persons with gametids. Let b be the proportion of these (say 1/4) which succeed in biting; s the proportion (say 1/3) which succeed in maturing the parasites; and b the proportion which succeed in biting another person. Then $bsbaimp$ gives the number of Anophelines which succeed in infecting persons.

We have assumed that $b = 1/4$, $s = 1/3$, $i = 1/4$; so that if each of these bites a different person, we shall have—

$$\text{No. of inoculations} = b^2saimp = amp/192$$

$$\text{Inoculation rate } \% = \frac{amp}{192} \cdot \frac{100}{p} = \text{about } \tfrac{1}{2}\, am.$$

That is to say, the inoculation rate per 100 of population equals about half the malaria ratio (m) multiplied by the mosquito ratio (a).

For example, in a village containing 1,250 people, 750 infected people, and 3,000 Anophelines, $p = 1{,}250$, $m = 0{\cdot}6$, $a = 2{\cdot}4$; and we calculate roughly that the number of infecting Anophelines, and also of inoculations, will be about 9·4. The inoculation rate per cent. will be about $1/2\ (2{\cdot}4 \times 0{\cdot}6) = 0{\cdot}72$; that is, the chances of being inoculated in the village will be as 72 is to 10,000.

Or suppose that in another village half the people are infected, and there are about twenty Anophelines to each person. Then the chances of becoming infected there will be about 5/100.

Such calculations may appear far-fetched to many; but they are useful, not so much for the numerical estimates yielded by them, but because they give more precision to our ideas, and a guide for future investigations.

Laws which Regulate the Amount of Malaria in a Locality.—The number of infecting mosquitos which succeed in biting again is b^2saimp. If all of these bite different people, and all these people are healthy, and all become infected, this expression will also denote the number of *new infections* occurring in the locality. But, of course, the infecting mosquitos may often happen to bite on the second occasion, not healthy persons, but persons already infected, especially if the proportion of the latter is large.

If, as before, mp denotes the number of persons already infected at the beginning of the enquiry, then $p - mp$ or $(1 - m)\,p$ denotes the number of healthy people. Hence by proportion

the number of infecting mosquitos which bite healthy persons (on the second biting) will be x, where

$$x : b^2saimp :: (1-m)\,p : p$$

or
$$x = b^2sai\,(1-m)\,mp \quad . \quad . \quad . \quad . \quad (1)$$

and if each bites a different person and each person becomes infected, the same expression will denote the number of *new infections* which occur in the locality—that is, will denote the addition to the number of malaria cases there.

But this is not the whole change which may occur. While, during the period of observation, new infections are being produced, it may happen that some of the old cases may have recovered. The number of those old cases was originally mp: let rmp denote the number of those who have recovered during the period of observation—so that r is a fraction. Hence the whole number of cases in the locality will have increased or decreased at the end of the period of observation, according to whether $b^2sai\,(1-m)\,mp$, the number of new cases, is greater or less than rmp, the number of recoveries. Thus (neglecting common factors) the change depends upon whether $b^2sai\,(1-m)$ is greater or less than r.

Suppose that no change occurs—that the recoveries exactly equal the new infections. Then

$$b^2sai\,(1-m) = r \quad . \quad . \quad . \quad . \quad (2)$$

From this equation we can calculate the values of a and m when the amount of malaria in the locality remains constant—that is, if we know the values of b, s, i, and r.

Suppose that the period of observation is one month. Now, in section 21, I estimated roughly that only about half the cases of malaria remain infected after three months. If this rate holds for smaller periods, we may suppose that the ratio of people who remain infected after only one month will be given by the cube root of 1/2—that is, by 0·7937; so that the proportion of those who recover in one month will be 1−0·7937. That is, we may write $r = 0{\cdot}2063$. Let us take the values of b, s, i as suggested in the previous section—so that $b^2si = 1/192$.

Hence the new infections will equal the recoveries if

$$a(1-m) = 192 \times 0{\cdot}2063 = 39{\cdot}59 = 40 \text{ (\textit{say})} \quad . \quad . \quad . \quad (3)$$

and the malaria will increase or diminish in the locality according to whether $a(1-m)$ is greater or less than 40. Thus, if m, the original malaria rate, is very small, the malaria will not increase unless a, the monthly number of Anophelines per head of human population, is greater than 40. On the other hand, if m is a larger fraction, say 1/2, the malaria will not increase unless a is greater than 80. If m is still larger, say 3/4, the malaria will not increase unless a is greater than 160. This suggests that the malaria rate is not likely to increase indefinitely unless the number of mosquitos is enormous. On the other hand, if the number of Anophelines is below the figure given by the equation, the malaria rate ought to begin to fall, *because the new infections can no longer keep pace with the recoveries.*

It should be noted that by the number of Anophelines we here mean the number of *different* Anophelines which may bite each person *during a whole month*, and not the insects which may be, so to speak, allotted to each person at any one moment. We say one month because this is the period we have selected for observation — the period during which we suppose that 0·2 or 1/5th of the cases recover. If we had selected one week for the period of observation, the proportion of recoveries would, of course, be lower (about 0·056142), and the number of different Anophelines to each person, required to compensate for the recoveries during the week, would be correspondingly less (as shown by the equation).

Now, what will happen if the malaria rate, instead of remaining constant, increases or decreases? On the one hand, will it increase until every one becomes infected; or, on the other hand, will it decrease until it vanishes?

We have supposed that mp denotes the number of cases at the beginning of the enquiry, which lasts, let us say, for a month. Let m_1p, m_2p, m_3p . . . denote the number of cases

at the end of 1, 2, 3 . . . months respectively. Then if the other figures remain constant, we have,

$$m_1 p = \textit{original cases} + \textit{new infections} - \textit{recoveries}$$
$$= mp + b^2 sai\,(1-m)\,mp - rmp \quad . \quad . \quad . \quad . \quad . \quad (4)$$

and as the same process repeats itself month after month we continue to have,

$$m_2 p = m_1 p + b^2 sai\,(1-m_1)\,m_1 p - rm_1 p$$
$$m_3 p = m_2 p + b^2 sai\,(1-m_2)\,m_2 p - rm_2 p$$
$$. \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad .$$

and so on. We can calculate m_1 from the first equation. Substituting its value in the second equation we calculate m_2; and substituting this in the third equation we calculate m_3; and so on indefinitely.

If $r = 0{\cdot}2$ and $b^2 si = {\cdot}005$, the value of the *nth* term of the series $m_1 p$, $m_2 p$ . . . $m_{n-1} p$, $m_n p$ may be written

$$m_n p = (160 + a - am_{n-1})\,m_{n-1}\,p \times 0{\cdot}005 \quad . \quad . \quad . \quad (5)$$

Let us now consider for examples the case of a village containing 1,000 people of whom half are infected at the beginning of the enquiry. By equation (3) of this section, and also by this equation, if the number of different Anophelines *per* person during one month (a) is 80, the malaria will neither increase nor decrease, so that m_n will always be the same as m, namely, 0·5. But if a is greater or less than this, the malaria will increase or decrease accordingly.

(1). First, suppose that there are 100 different Anophelines *per* person during a month—so that the malaria should increase. Thus we calculate,

$$m_1 p = (160 + 100 - 100 \times 0{\cdot}5) \times 5 \times 0{\cdot}5 = 525$$
$$m_2 p = (160 + 100 - 100 \times 0{\cdot}525) \times 5 \times 0{\cdot}525 = 544{\cdot}5.$$

Proceeding in this way we find that the number of cases should increase every month as follows:—

Increase of Cases with 100 *Anophelines*

Months	0	1	2	3	4	.	.	.	*finally*
Cases	500	525	544	560	571	.	.	.	600

But how do we reach the last figure? As we calculate the number of cases month after month we observe that they always increase, but by a constantly decreasing increment. Finally, this increment becomes very small, so that the number of cases *approaches a fixed limit.* It is easy to calculate this limit mathematically (as will be done presently), but we can also calculate it very simply as follows. If the number of cases does ever arrive at a fixed limit, so that it no longer increases, then equation (3) of this section must hold; that is, the number of cases and the number of mosquitos will be exactly balanced according to the formula $a\ (1-m)=40$. From this we have, when this exact balance is reached,

$$m=1-40/a \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Here $a=100$; so that finally $m=1-0{\cdot}4=0{\cdot}6$; which, when multiplied by the population (1,000), gives 600 cases as the final limit.

(2). Next, suppose that there are only 60 Anophelines *per* person. Then we calculate as before,

Decrease of Cases with 60 *Anophelines*

Months	0	1	2	3	4	. . .	*finally*
Cases	500	475	455	438	424	. . .	333

The final result is obtained as before from equation (6). Here then, although the malaria ratio diminishes rapidly at first, it never disappears altogether, but ultimately stands at 1/3 of the population.

(3). Next suppose that there are 40 Anophelines *per* person.

Decrease of Cases with 40 *Anophelines*

Months	0	1	2	3	4	. . .	*finally*
Cases	500	450	409	376	348	. . .	0

Here the fall is quicker and the malaria finally vanishes, because $m=1-40/40=0$; but very many months will elapse before this result is approached.

(4). We also have

Decrease of Cases with 1 *Anopheline per head.*

Months	0	1	2	3	4	. . .	*finally*
Cases	500	401	322	259	207	. . .	0

(5) *Decrease of Cases with no Anophelines.*

Months	0	1	2	3	4	. . .	*finally*
Cases	500	400	320	256	205	. . .	0

Thus the presence of only a small number of Anophelines does not affect the result very much. In fact we can see this from the form of the equation (5), namely,

$$m_n p = \{160 + a(1 - m_{n-1})\} m_{n-1} p \times 0{\cdot}005,$$

because $1 - m_{n-1}$ is always a fraction, and a must therefore be a considerable number if it is to have any marked effect compared with the first term 160.

Returning now to the subject of the *limit* mentioned in example (1). It is known in mathematics that if a series such as m_1, m_2, m_3 . . . here considered tends to a limit, that limit can often be easily found. Let m denote the limit—that is, $m = m_n$ when n, the number of terms, is indefinitely increased, In other words, m is the malaria ratio which is *finally* arrived at after the lapse of many months.

Now we had in equation (4),

$$m_n p = \{1 + b^2 sai\,(1 - m_{n-1}) - r\} m_{n-1} p$$

By the mathematical rule referred to, the value of m_n, or m, can be easily found, when n is large, by solving the equation

$$mp = \{1 + b^2 sai\,(1 - m) - r\} mp$$

that is,

$$m = 1 - r/b^2 sai \quad . \quad . \quad . \quad . \quad . \quad (7)$$

If $r = 0{\cdot}2$ and $b^2 si = 1/200$, this gives $m = 1 - 40/a$, which is the same as equations (2) and (3), which have already been used to find the limit shown in example (1). There we calculated the limit by another line of reasoning, but now we see that it can be obtained also by the ordinary mathematical rule. (This rule is that if $\phi^n x$ is a repeated function of x, its value when n

is indefinitely large will often be given by the roots of the equation $x = \phi x$).

The reader should make a careful study of those ideas, and will, I think, have little difficulty in understanding them, though he may have forgotten most of his mathematics. If our reasoning has been correct and complete enough, the main principles involved may be stated as follows:—

(1). Whatever the original number of malaria cases in the locality may have been, the ultimate endemic malaria ratio will tend to settle down to a fixed figure, dependent on the number of Anophelines and the other factors — that is, if these factors remain constant all the time.[1]

(2). If the number of Anophelines is sufficiently high, the ultimate malaria ratio (m) will become fixed at some figure between 0 and 1 (that is, between 0% and 100%). If the number of Anophelines is sufficiently low (say below 40 *per* person), the ultimate malaria rate will tend to zero—that is, the disease will tend to die out. (In this calculation a *negative* malaria ratio, that is, one which is less than nothing, must be interpreted as meaning zero).

Consider, for example, the case of a village with 1,000 inhabitants and 60 different Anophelines for each person during one month. If, to begin with, every person starts with being infected, then the malaria ratio will fall month by month until it reaches the value $m = 1 - 40/60$; that is, until 333 persons are left infected. And this occurs because there are not enough Anophelines to maintain the original high rate of 100% infection. But now suppose that with the same number of people and of Anophelines, the epidemic began with only one infected person from outside: the number of Anophelines

[1] This is a well-known peculiarity of repeated functions. See, for instance, my paper "A Method of solving Algebraic Equations," *Nature*, 29th October 1908, p. 663.

will now be too large to allow this original low rate of 0·1% infection to continue, and the rate will consequently rise until the value $m = 1 - 40/60$, giving 333 infected persons, is reached. Thus, whether every one, or only one person, is infected to start with, the ultimate result will be the same—the number of cases will be 333, and will continue at that figure so long as all the factors remain the same. That is, an exact balance between the number of cases and the number of Anophelines will be arrived at. Many months may, however, elapse before this happens.

Suppose that all the factors b, s, i, a, r do *not* remain the same. Then if any of them is temporarily altered a corresponding change will be made in the rate of increase or decrease; but after the temporary disturbance has ceased, things will again tend to return to the normal state—just as water always seeks to find its own level. Thus, if the recovery rate r is increased by a temporary administration of quinine, or the number of mosquitos a is temporarily diminished by winter or by active "petrolage," a change for the better will be made, but it will cease soon after these alterations cease. If, however, the alteration is permanent, then the value of m will, of course, be permanently affected by it.

We have often assumed certain *conjectural* values for some of the factors; does this fact invalidate the reasoning? We will examine these values more closely in the next section, but the exact figures do not affect the general law. We have supposed that, in equation (7), $r/b^2si = 40$; from which we argued that the ultimate malaria ratio will vanish if the number of different Anophelines to each person is less than about 40 *per* month. The actual number may be more or less, but the fact that a limit must be reached remains. As I have said, the whole calculation is useful, not so much for its numerical results, but because it gives precision to our ideas.

A more serious objection is that, in framing the fundamental equation (4), we have disregarded certain factors which would modify it. For example, the population will be subject

to constant changes owing to immigration, emigration, births and deaths—all of which operate both on the healthy and on the infected. Thus the birth-rate will give a continuous supply of healthy individuals, while the death-rate will remove many of the infected ones. Also many of the recovered cases, and many of the mosquitos, may be at least partially immune; gametids may appear in the blood more during some seasons than during others, and infected mosquitos may bite many more than one person each; but the introduction of all these factors would give a much more complicated equation than we have need for here. It will still be of the form

$m_1 p = original\ cases + new\ infections - recoveries$ (*or deaths*),

and from this we shall still be able to argue that a limit must be reached when the new infections exactly balance the recoveries. We may therefore conclude,

(1) That the amount of malaria in a locality *tends* towards a fixed limit determined by the number of malaria-bearing mosquitos and by other factors.

(2) That if the number of malaria-bearing Anophelines is below a certain figure, that limit will be zero.

It is often thought and said that malaria should exist wherever susceptible Anophelines exist, and that anti-mosquito measures will therefore be useless so long as any of these insects remain. But more careful reasoning will convince us that malaria cannot persist in a community unless the Anophelines are so numerous that the number of new infections compensates for the number of recoveries.